EXHIBIT 8

National Institute of Environmental Health Sciences
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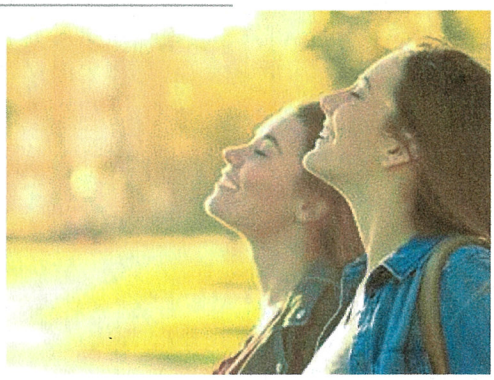
Gene and Environment Interaction

Introduction



Few diseases result from a change in a single gene or even multiple genes. Instead, most diseases are complex and stem from an interaction between your genes and your environment. Factors in your environment can range from chemicals in air or water pollution, mold, pesticides, diet choices, or grooming products.

Subtle differences in one person's genes can cause them to respond differently to the same environmental exposure as another person. As a result, some people may develop a disease after being exposed to something in the environment while others may not.

As scientists learn more about the connection between genes and the environment, they pursue new approaches for preventing and treating disease that consider individual genetic codes.

What Is NIEHS Doing?

NIEHS studies a wide range of diseases and disorders with genetic and environmental components. In addition, new technologies and computational approaches are under development to tease out the gene and environment interactions that underpin disease.

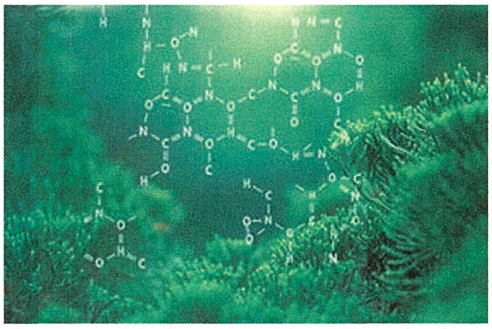
- Adult & Juvenile Myositis *(https://joinastudy.niehs.nih.gov/studies/myopathies/index.htm)*
- Calcinosis Study *(https://joinastudy.niehs.nih.gov/studies/calcinosis/index.htm)*
- EPR: DNA & Your Environment
- MYORISK Study *(https://joinastudy.niehs.nih.gov/studies/myorisk/index.htm)*

- **Autism** *(https://www.nih.gov/health/topics/conditions/autism/index.cfm)* - High levels of air pollution increase the risk for autism in children with a genetic variant called MET, which is involved in brain development. [1] This genetic variant did not increase the risk for the 75% of the population exposed to lower levels of air pollution, suggesting that autism may be caused by an interaction of genetic and environmental factors.
- **DNA Repair** *(https://www.nih.gov/research/supported/health/dna-repair/index.cfm)* - Molecules damaged by environmental exposures like ultraviolet light or certain chemicals are incorporated into DNA, triggering cell death that may lead to cancer, diabetes, hypertension, cardiovascular and lung disease, and Alzheimer's disease. [2]
- **Metabolism** - Researchers in the NIEHS Metabolism, Genes, and Environment Group *(https://www.nih.gov/research/atniehs/labs/stl/pi/metabolism/index.cfm)* discovered that a protein called SIRT1,

which plays a critical role in early development and metabolism, could provide the basis for therapeutic targets for metabolic diseases and aging at the genetic level. [3]

- **Parkinson's disease** *(https://www.nih.gov/health/topics/conditions/parkinson/index.cfm)* - The chance of developing Parkinson's disease after pesticide exposure was greater in people who had a genetic variation that affected the production of nitric oxide, a molecule that can damage neurons. [4] Lifestyle choices related to diet, exercise, and nicotine use also have been linked to the chance of developing Parkinson's disease.
- **Respiratory Syncytial Virus (RSV)** - An international study that included NIEHS scientists discovered children with variations in a gene called TLR4 who were exposed to certain environmental factors developed severe cases of RSV bronchiolitis, a life-threatening respiratory disease. [5]

New data analysis methods – Many studies can only analyze one type of environmental exposure at a time, which does not account for combined effects of multiple exposures and genes acting together. But, a computational approach by NIEHS-funded researchers can simultaneously analyze data on multiple environmental exposures and their interactions with genes. [6] Researchers used data about atherosclerosis, a chronic heart condition, as a test case for the method's application in future studies.



Monitoring the state of the field – NIEHS helped convene a workshop, "Current Challenges and New Opportunities for Gene-Environment Interaction Studies of Complex Diseases," to explore issues surrounding study of the interplay between genes and the environment. [7] Attendees found that along with research challenges many exciting opportunities exist for new studies.

Further Reading

Stories from the *Environmental Factor* (NIEHS newsletter)

- Cumulative Exposures, Precision Medicine Focus of Mayo Conference *(https://factor.niehs.nih.gov/2022/12/feature/1-feature-individualized-medicine/index.htm)* (December 2022)
- Environmental Exposures and Parkinson's Disease: Connecting the Dots *(https://factor.niehs.nih.gov/2022/12/feature/4-feature-parkinsons-disease/index.htm)* (December 2022)
- NIEHS Helps Sow Seeds of African Gene-environment Research *(https://factor.niehs.nih.gov/2022/8/feature/2-feature-h3africa-biorepositories/index.htm)* (August 2022)
- Ethical Issues Emerge in Gene-environment Interactions Research *(https://factor.niehs.nih.gov/2022/2/feature/2-feature-research-ethics/index.htm)* (February 2022)
- Data Science May Resolve How Environment Influences Disease *(https://factor.niehs.nih.gov/2021/1/science-highlights/data-science/index.htm)* (January 2021)
- Bold Plan to Study Gene-environment Interactions Presented to Council *(https://factor.niehs.nih.gov/2020/7/science-highlights/exposome/index.htm)* (July 2020)

Additional Resources

- Human Genome Project *(https://www.genome.gov/genetics-glossary/human-genome-project)* (National Institutes of Health)

Related Health Topics

- Endocrine Disruptors *(https://www.nih.gov/health/topics/agents/endocrine/index.cfm)*
- Exposure Science *(https://www.nih.gov/health/topics/science/exposure/index.cfm)*
- Toxicology *(https://www.nih.gov/health/topics/science/toxicology/index.cfm)*

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4. Paul KC, Sinsheimer JS, Rhodes SL, Cockburn M, Bronstein J, Ritz B. 2016. Organophosphate Pesticide Exposures, Nitric Oxide Synthase Gene Variants, and Gene-Pesticide Interactions in a Case-Control Study of Parkinson's Disease, California (USA). Environmental Health Perspectives. 124(5):570-7. [Abstract *(https://www.ncbi.nlm.nih.gov/pubmed/26383258)*]
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6. Ko YA, Mukherjee B, Smith JA, Kardia SL, Allison M, Diez Roux AV. 2016. Classification and Clustering Methods for Multiple Environmental Factors in Gene-Environment Interaction: Application to the Multi-Ethnic Study of Atherosclerosis. Epidemiology 27(6):870-878. [Abstract *(https://www.ncbi.nlm.nih.gov/pubmed/27479650)*]
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